

Remarks

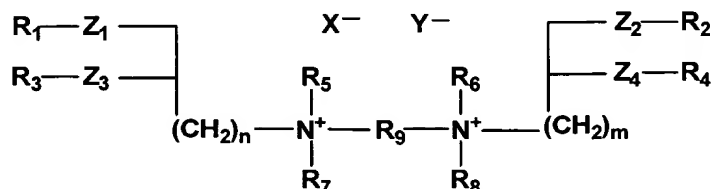
Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 47-94 are pending in the application, with 47 and 83 being the independent claims. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Description of the Invention

The present invention is directed to particular cationic compounds, compositions comprising said cationic compounds, methods of using said cationic compounds, and pharmaceutical kits comprising said cationic compounds. Specifically, the cationic compounds of the present invention are cationic dimers having the following formula:



wherein R_1 - R_9 , Z_1 - Z_4 , n , m , X^- and Y^- are defined therein. The cationic dimers of the present invention are useful for, *inter alia*, enhancing the delivery of biologically active compounds

to a cell. More particularly, R_9 is a linker moiety which is selected from a group of moieties as described in the present patent application.

Objection to the Claims

The Examiner has objected to claim 82 and dependents because the claims recite non-elected subject matter, specifically a method of delivering a biologically active agent to a plant cell. Applicant has amended claim 82 and submits that claim 82 is directed to elected subject matter. Applicant submits that the Examiner's objection to claim 82 has been accommodated.

Rejections under 35 U.S.C. § 112

The Examiner has rejected claims 47-49, 68-70, and 74-76 under 35 U.S.C. § 112, first paragraph, as containing new matter. Specifically, the Examiner contends that the proviso added by amendment, "provided that R_9 is not C_3 to C_{22} unsubstituted alkyl," was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention at the time the application was filed. Applicant respectfully traverses the rejection.

Applicant previously amended the definition of R_9 in an attempt to distinguish the present invention from certain compounds that appear to be disclosed in a previously cited reference. As discussed in the Amendment and Reply filed April 19, 2002, Bhattacharya *et al.*, *Chem Commun.* (23):2287-2288 (1997) appears to disclose certain compounds within the scope of originally filed claim 1. Applicant filed the earlier amendment previous to any




substantive examination in order to facilitate prosecution of the present application. The Examiner contends that there is no apparent support for the amendment in the specification.

Solely in order to further the prosecution of the present application, Applicant has amended claim 1 so that the proviso is limited to the eight relevant compounds which appear to be disclosed in Bhattacharya *et al.* Applicant submits that the present application provides the required written description for amended claim 1.

The Federal Circuit has recognized that "[i]nventions are constantly made which turn out not to be patentable, and applicants frequently discover during the course of prosecution that only a part of what they invented and originally claimed is patentable." *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976). An applicant for a patent has the right to claim less than the full scope of one's disclosure. *In re Johnson*, 558 F.2d 1008, 194 USPQ 187 (CCPA 1977). The mere removal of a few compounds from a genus, in order to excise the invention of another, is not considered new matter. *Id.* at 1018, 194 USPQ at 196.

Here, Applicant has merely excised the few species which appear to be disclosed in Bhattacharya *et al.* in order to define clearly his claimed invention. The many examples of specific compounds provided in the present application fall within the narrowed genus of amended claim 1. Thus, the present specification "contains a broad and complete generic disclosure, coupled with extensive examples fully supportive of the limited genus now claimed." See *id.* at 1018, 194 USPQ at 196.

Furthermore, the subject matter of claims 48 and 49 does not permit the linker, R₉, to be unsubstituted alkyl. That is, R₉ according to claim 48 comprises C₁ to C₁₀ substituted alkyl, C₁ to C₁₀ alkenyl, or C₁ to C₁₀ substituted alkenyl, and R₉ according to claim 49 further comprises a peptide linkage. Even if there is a question as to the alleged new matter of



claim 47, the proviso of claim 47 is not applicable to claims 48 and 49. Therefore, Applicant submits that claims 47 and 48 do not contain new matter.

In view of the above arguments, Applicant asserts that claims 47-49, 68-70, and 74-76 are not unpatentable under 35 U.S.C. § 112, first paragraph, and respectfully requests reconsideration and withdrawal of the rejection of claims 47-49, 68-70, and 74-76 under 35 U.S.C. § 112, first paragraph.

The Examiner has rejected claims 47-49, 68-70, 74-86, 93, and 94 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter. Specifically, the Examiner has alleged that the term "non-toxic anions" does not have clear metes and bounds. Applicant respectfully traverses the rejection.

The second paragraph of 35 U.S.C. § 112 requires that the specification conclude with one or more claims that "particularly point[] out and distinctly claim[] the subject matter which applicant regards as his invention." 35 U.S.C. § 112. The definiteness inquiry focuses on whether one of ordinary skill in the art would comprehend the scope of the claim when read in light of the rest of the specification. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). When determining compliance with 35 U.S.C. § 112, second paragraph, the claim language must be analyzed in light of a) the content of the specification of the application; b) the teachings of the prior art; and c) the claim interpretation that would be given by one of ordinary skill in the art.



Moreover,

[i]f the scope of subject matter embraced by a claim is clear, and if the applicant has not otherwise indicated that he intends that claim to be of a different scope, then the claim does particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

In re Borkowski, 422 F.2d 904, 909, 164 USPQ 642, 645-646 (CCPA 1977).

The term "non-toxic" is a well-known term in the field of pharmaceuticals. Contrary to the Examiner's contention, the term is used in the art with a well understood meaning. The term "non-toxic" is used in a number of issued U.S. patents. See, *e.g.*, U.S. Patent Nos. 6,448,259; 6,448,290; and 5,459,127. Likewise, the term "toxic," which is antonymous to non-toxic, is frequently used in the art. Claims are not indefinite if they reasonably apprise those of ordinary skill in the art and are as precise as the subject matter permits. *Hybritech Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). Moreover, "[t]echnical terms are not per se indefinite when expressed in qualitative terms without numerical limits." *Modine Mfg. Co. v. U.S. Int'l Trade Comm'n*, 75 F.3d 1545, 1557, 37 USPQ2d 1609, 1617 (Fed. Cir. 1996), *cert. denied*, 116 S. Ct. 2523 (1996). The particular field of research lends itself to terms that may not be as precise as one would like.

As the Examiner concedes, any anion could be non-toxic if present in sufficiently small amounts. Fortunately, the field of toxicological research recognizes this fact. Toxicologists have several, well-known methods to determine whether a given amount of a particular anion is toxic or non-toxic. Furthermore, the U.S. Food and Drug Administration (FDA) provides guidance regarding the determination of potential toxicity




of new pharmaceuticals. Food and Drug Administration, HHS, 21 CFR § 312.23(a)(8)(ii)(a); see, *e.g.*, Exhibit A.

"A patent applicant is free to recite features of an apparatus either structurally or functionally." *In re Swinehart*, 439 F.2d 210, 212, 169 USPQ 226, 228 (CCPA 1971). In the present case, Applicant has merely opted to define his invention both structurally and functionally. Applicant has defined the structure of the novel cationic lipid molecule. The novelty of the invention lies in the structure of this lipid and its compositions and uses. In addition, Applicant has used a well-known term of the art to define which anions are within the scope of the invention. The issue presented is comparable to a claim which utilizes the phrase "a pharmaceutically effective amount." Such a phrase, although not reciting a precise number or limitation, is not considered indefinite by one of ordinary skill in that art. Accordingly, the term "non-toxic" apprizes those of ordinary skill in the art and, therefore, is not indefinite.

In view of the above arguments, Applicant asserts that claims 47-49, 68-70, 74-86, 93, and 94 are not unpatentable under 35 U.S.C. § 112, second paragraph, and respectfully requests reconsideration and withdrawal of the rejection of claims 47-49, 68-70, 74-86, 93, and 94 under 35 U.S.C. § 112, second paragraph

Rejections under 35 U.S.C. § 102

The Examiner has rejected claims 47-49 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 3,983,079 ("the '079 patent"). Specifically, the Examiner asserts that the '079 patent "teaches a composition according to the structure recited in

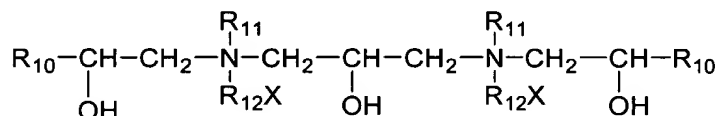


instant claims 47 and 48, wherein R₉ is the substituted alkyl group CH₂-CHOH-CH₂."

Applicant respectfully traverses the rejection.

The Examiner points to column 3, lines 60-65 of the '079 patent as supporting his conclusion that the '079 patent teaches a composition according to the present invention. The '079 patent discloses a broad genus of compounds that are useful in detergent compositions. (The '079 patent, col. 2, ll. 28-65). The specific examples to which the Examiner refers are described as follows.

Specific examples of compounds having two quaternary ammonium groups, and two long aliphatic hydrocarbon radicals are represented by the formula:



wherein R₁₀ is an alkyl radical containing from 6 to about 20, preferably 10 to 14, carbon atoms, and R₁₁ and R₁₂ are methyl, ethyl or hydroxyethyl, and the cation X⁺ is a chloride or bromide.

(The '079 patent, col. 3, line 58, to col. 4, line 2.)

The present invention is distinguished from the compounds of the '079 patent in that the prior art compounds require R₁₀ to be an alkyl radical containing from about 6 to about 20 carbon atoms. The novel compounds of the present invention require hydroxy, ether, or ester substituents at the same position as R₁₀, *i.e.*, R₁-Z₁- or R₂-Z₂- is a hydroxy, ether, or ester group. Applicant respectfully submits that the '079 patent does not teach a compound according to the present invention and, therefore, the present invention is not anticipated by the '079 patent. Furthermore, the '079 patent does not provide any teaching or suggestion to make a compound of the present invention.

In view of the above arguments, Applicant asserts that claims 47-49 are not anticipated under 35 U.S.C. § 102(b) by the '079 patent and respectfully requests reconsideration and withdrawal of the rejection of claims 47-49 under 35 U.S.C. § 102(b).

Rejections under 35 U.S.C. § 103

The Examiner has rejected claim 83 under 35 U.S.C. § 103(a) as being obvious over the '079 patent. According to the Examiner, the '079 patent teaches a composition according to instant claim 83 and it would have been obvious to one of skill in the art to store said composition in a container. Applicant respectfully traverses the rejection.

As explained above, the '079 patent does not teach a compound having the structure of the present invention. In view of the teaching of the '079 patent, it would not have been obvious to one of ordinary skill in the art to make the novel compounds of the present invention. Accordingly, it would not have been obvious to make the kit according instant claim 83. Therefore, the claimed invention is nonobvious and patentable.

In view of the above arguments, Applicant asserts that claim 83 is not obvious under 35 U.S.C. § 103(a) in view of the '079 patent and respectfully requests reconsideration and withdrawal of the rejection of claim 83 under 35 U.S.C. § 103(a).

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Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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Date: October 25, 2012

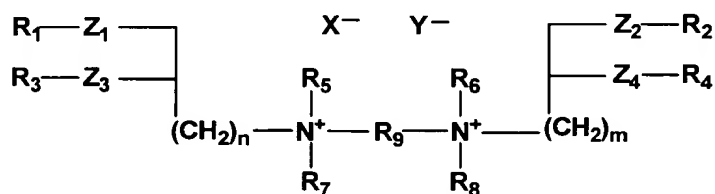
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Version with markings to show changes made

47. (New) A cationic lipid compound of the following formula



wherein

Z_1, Z_2, Z_3 and Z_4 are the same or different and are $-O-C(O)-$ or $-O-$;

R_1 and R_2 are the same or different and are H, C_1 to C_{24} alkyl or C_1 to C_{24} alkenyl;

R_3 and R_4 are the same or different and are C_1 to C_{24} alkyl or C_1 to C_{24} alkenyl;

R_5, R_6, R_7 and R_8 are the same or different and are H, C_1 to C_{10} alkyl or C_1 to C_{10}

alkenyl;

R_9 is a linker;

n and m are the same or different and are 1 to 8; and

X and Y are the same or different and are non-toxic anions;

provided that when R_9 is a straight-chain alkylene having 3-6, 12, 16, 20, or 22 carbons, then all of R_1, R_2, R_3 , and R_4 are not H, all of R_5, R_6, R_7 , and R_8 are not methyl, m and n are not 1, and Z_1, Z_2, Z_3 , and Z_4 are not O [not C_3 to C_{22} unsubstituted alkyl].

82. (Once Amended) A method for delivering a biologically active agent to a cell of [a plant or] an animal, said method comprising:

contacting said cell with a lipid aggregate, said lipid aggregate comprising said
biologically active agent and a compound of claim 47.

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Version with markings to show changes made

Claims 1-46 are canceled.

Claims 47-94 are new.

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